Assessment of HIV-positive Patients

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Outline of this Unit

- Considerations for the Initial assessment of an HIV-positive patient
- What HIV-related tests need to be done at baseline?
- Recommended Immunizations for HIV positive individuals
- When prophylaxis for opportunistic infections (OIs) are recommended

Initial assessment of an HIV-positive patient

Comprehensive past & present medical history I

These are some of the main topics to assess in the medical history of an HIV positive patient:

- **Comorbidities**: history of and risk factors for coronary heart disease, dyslipidemia, diabetes, hypertension, asthma, COPD, kidney disease, and osteoporosis.
- **Psychiatric history:** treatment for or symptoms of depression, anxiety, suicidal ideation, or posttraumatic stress disorder, psychiatric hospitalizations .etc.
- **Sexually transmitted diseases**: gonorrhea, chlamydia, pelvic inflammatory disease, chancroid, syphilis, herpes simplex virus, HPV, and trichomoniasis, including treatment history and outcome
- **Viral Hepatitis:** Hepatitis A, B, C. Most recent serology results and immunizations
- **History of Tuberculosis** (TB) exposure, most recent PPD test, and/or prior TB treatments

Comprehensive past & present medical history II

- **Women**:
  - gynecologic and obstetric history,
  - plans for future pregnancy, birth control practices,
  - last Pap test, abnormal Pap test ever
  - menstrual history
  - mammogram (if applicable)

- **Medications** :
  - Current medications, including over-the-counter medications. Use of complementary or alternative therapy or treatment .
  - History of previous Antiretroviral Treatment (ARTs). History of ART intolerance or treatment failures

- **Psychosocial History:**
  - Present or past history of substance use (smoking, alcohol, drugs)
  - Social history, including work and immigration status. Social support and partner HIV status.
  - Disclosure to partner and HIV status.

- **Patient understanding of HIV infection, treatment plan and management**

Relevant Points of the HIV Related History

- HIV exposure history
  - Date and place of the diagnosis
  - Route of exposure, or risk factors.
  - History of acute HIV illness or seroconversion. It can generally present with fevers, soar throat, skin rash, fatigue, diarrhea, headache, etc.
- Prior history of receiving antiretroviral treatments. Which antiretroviral drugs , and causes for changes. Particularly intolerance or failures due to resistance.
- Most recent plasma viral load and CD_4 count results.
- Lowest CD_4 cell count (nadir CD_4) and highest (peak) viral load, including dates
- Prior history of opportunistic infections (OIs) or other HIV related illness or cancers. (See Appendix 1)

HIV Primary Care in Women

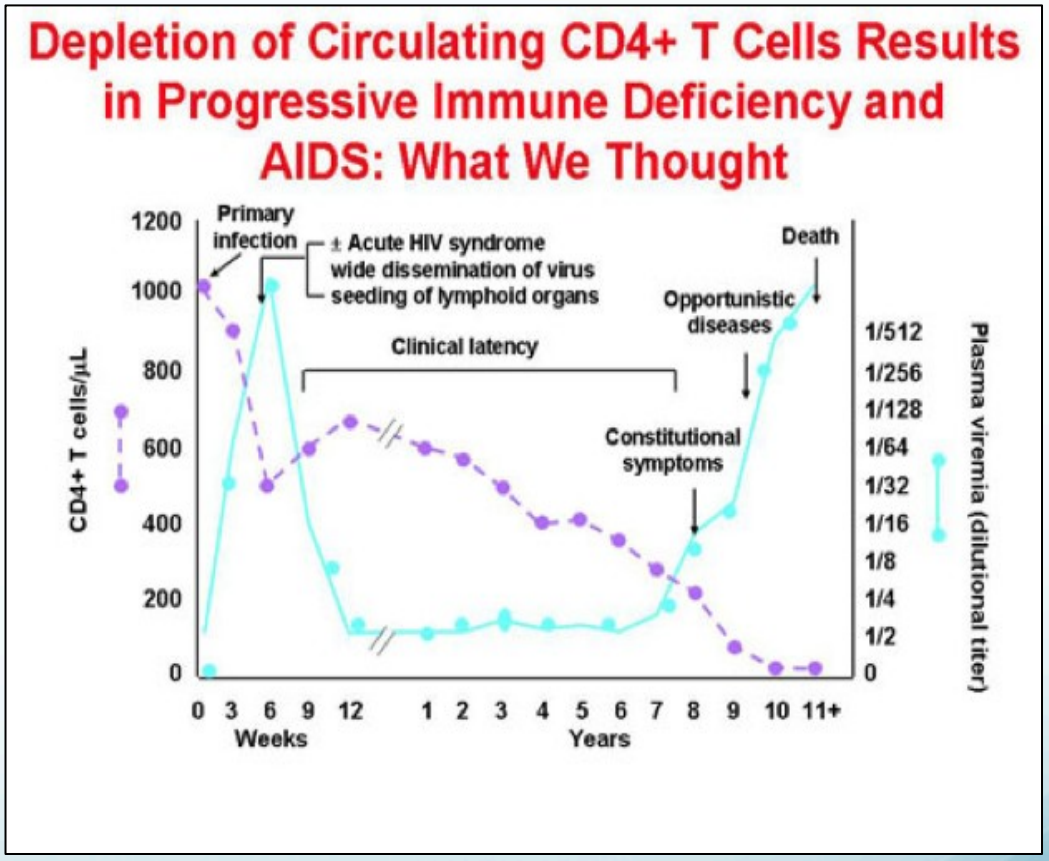
- All HIV positive women need a PAP smear at baseline and 6 months later.
  - If second PAP smear is normal, then annual follow-up
  - If PAP is abnormal, then colposcopy exam

- Screening mammography as recommended for non-HIV women.
- Bone mineral density (BMD) studies are recommended at age 50 or older and follow-up every 3 years for women and men. It can be done earlier if the patient had low trauma fractures or other risk factors.
- Consider referral to specialist in HIV-positive women, if patient is pregnant or desires to become pregnant.

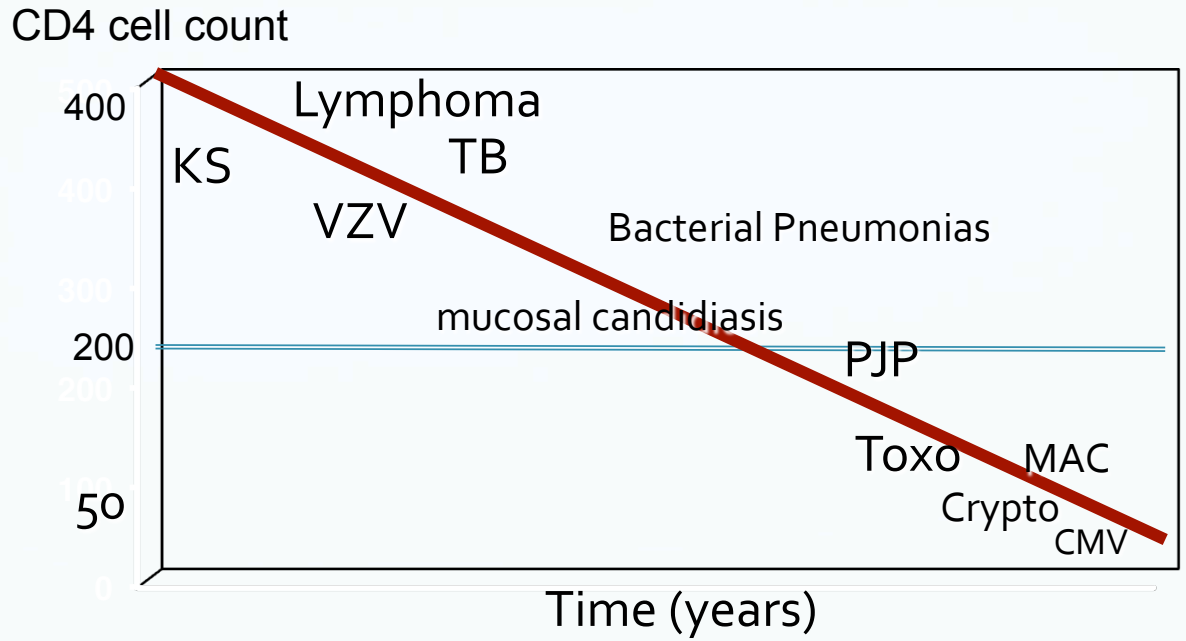
What HIV-related tests need to be done at baseline?

CD_4 Cell Count and Natural History of HIV Infection

- CD_4 cells are a type of white blood cells that are the main indicator of the immune function
- The most recent CD_4 count is the best predictor of disease progression
- CD_4 count helps to assess the response to treatments .
- There is a 30% variability in CD_4 results
- The CD_4s are reported as absolute count (normal range is : from 400 to 1200 c/ml) and as percentage or fraction (normal range is >27 %)



When do opportunistic diseases occur?



- Opportunistic infections (OIs) and HIV-related cancers can occur in patients who have not receive HIV treatment.
- Different OIs can occur at different CD4 levels
- Most of the OIs occur with CD4 below 200, including: PJP (formerly PCP), Mycobacterium Avium Complex (MAC) , Toxoplasmosis, Cryptococcal Meningitis, CMV retinitis, etc.
- Other HIV-related illnesses that occur with CD4s over 200 include Lymphoma, TB, Kaposi Sarcoma, bacterial pneumonias and Zoster infections.

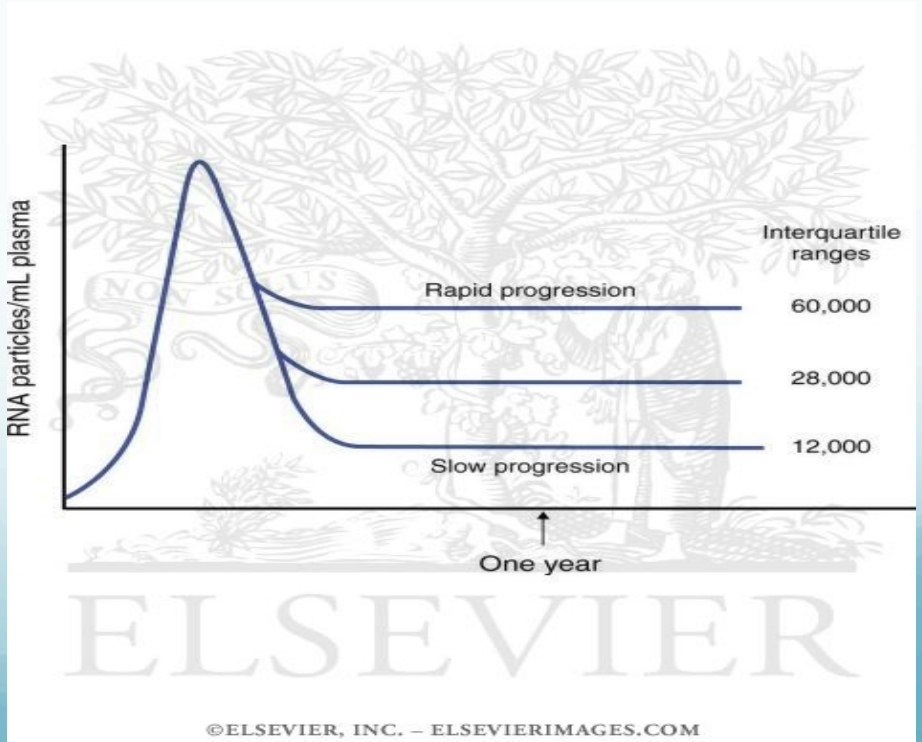
Viral Load Tests

- Viral load or plasma VL (pVL) is the number of copies of HIV RNA per mL in the plasma
- In untreated patients the pVL averages about 100,000 copies/mL of blood.
- It is an important predictor of disease progression and a direct measure of the effectiveness of antiretrovirals
- While on Antiretroviral Therapy the pVL should be <40 copies/ml or undetectable.

High
For example, greater than or equal to 100,000 copies/mL

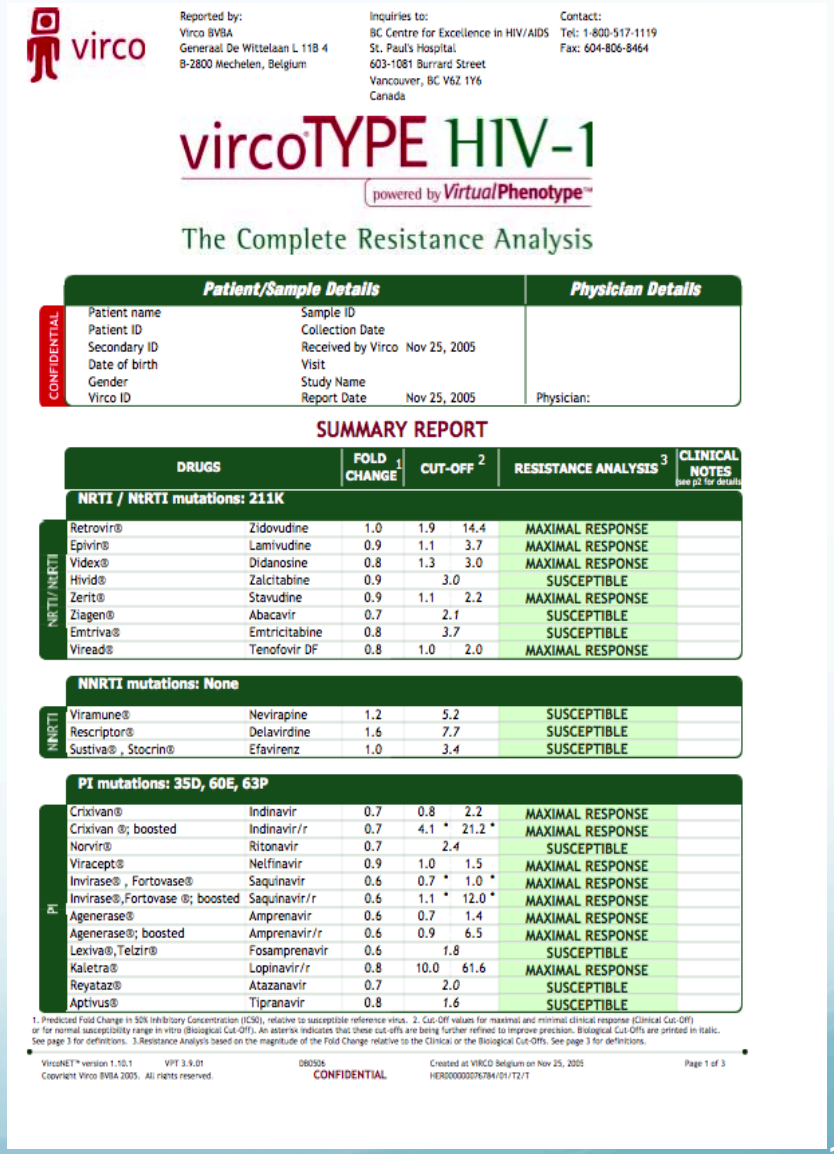
Low
For example, fewer than 10,000-30,000 copies/mL

Undetectable
For example, either less than 400 or less than 50 copies/mL, depending on the test used



HIV Resistance Testing or Genotype

- Should be done at baseline, to assess for primary resistance in all newly infected patients. *(Approximately 8% primary resistance in BC)*
- Should be repeated in the most recent pVL prior to initiation of ART
- Results will help to guide therapy
- Do a genotype test when the pVL rebounds ≥ 200 copies/ml on patients that were undetectable on ART.



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The Complete Resistance Analysis

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Patient/Sample Details			Physician Details
Patient name	Sample ID		
Patient ID	Collection Date		
Secondary ID	Received by Virco	Nov 25, 2005	
Date of birth	Visit		
Gender	Study Name		
Virco ID	Report Date	Nov 25, 2005	Physician:

SUMMARY REPORT

	DRUGS		FOLD CHANGE [1]	CUT-OFF [2]		RESISTANCE ANALYSIS [3]	CLINICAL NOTES (see p2 for details)
	NRTI / NtRTI mutations: 211K						
NRTI/NtRTI	Retrovir®	Zidovudine	1.0	1.9	14.4	MAXIMAL RESPONSE	
	Epivir®	Lamivudine	0.9	1.1	3.7	MAXIMAL RESPONSE	
	Videx®	Didanosine	0.8	1.3	3.0	MAXIMAL RESPONSE	
	Hivid®	Zalcitabine	0.9	3.0		SUSCEPTIBLE	
	Zerit®	Stavudine	0.9	1.1	2.2	MAXIMAL RESPONSE	
	Ziagen®	Abacavir	0.7	2.1		SUSCEPTIBLE	
	Emtriva®	Emtricitabine	0.8	3.7		SUSCEPTIBLE	
	Viread®	Tenofovir DF	0.8	1.0	2.0	MAXIMAL RESPONSE	
	NNRTI mutations: None						
NNRTI	Viramune®	Nevirapine	1.2	5.2		SUSCEPTIBLE	
	Rescriptor®	Delavirdine	1.6	7.7		SUSCEPTIBLE	
	Sustiva® , Stocrin®	Efavirenz	1.0	3.4		SUSCEPTIBLE	
	PI mutations: 35D, 60E, 63P						
PI	Crixivan®	Indinavir	0.7	0.8	2.2	MAXIMAL RESPONSE	
	Crixivan ®; boosted	Indinavir/r	0.7	4.1 *	21.2 *	MAXIMAL RESPONSE	
	Norvir®	Ritonavir	0.7	2.4		SUSCEPTIBLE	
	Viracept®	Nelfinavir	0.9	1.0	1.5	MAXIMAL RESPONSE	
	Invirase® , Fortovase®	Saquinavir	0.6	0.7 *	1.0 *	MAXIMAL RESPONSE	
	Invirase®,Fortovase ®; boosted	Saquinavir/r	0.6	1.1 *	12.0 *	MAXIMAL RESPONSE	
	Agenerase®	Amprenavir	0.6	0.7	1.4	MAXIMAL RESPONSE	
	Agenerase®; boosted	Amprenavir/r	0.6	0.9	6.5	MAXIMAL RESPONSE	
	Lexiva®,Telzir®	Fosamprenavir	0.6	1.8		SUSCEPTIBLE	
	Kaletra®	Lopinavir/r	0.8	10.0	61.6	MAXIMAL RESPONSE	
	Reyataz®	Atazanavir	0.7	2.0		SUSCEPTIBLE	
	Aptivus®	Tipranavir	0.8	1.6		SUSCEPTIBLE	

1. Predicted Fold Change in 50% Inhibitory Concentration (IC50), relative to susceptible reference virus. 2. Cut-Off values for maximal and minimal clinical response (Clinical Cut-Off) or for normal susceptibility range in vitro (Biological Cut-Off). An asterisk indicates that these cut-offs are being further refined to improve precision. Biological Cut-Offs are printed in italic. See page 3 for definitions. 3.Resistance Analysis based on the magnitude of the Fold Change relative to the Clinical or the Biological Cut-Offs. See page 3 for definitions.

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HLA-B*5701 Screening

- Abacavir is one on of the Antiretrovirals use as a backbone (NRT"s)
- The HLA-B 5701 is the test use to assess for Abacavir (ABC) hypersensitive reaction (HSR).
- Recommended in all HIV patients at baseline, and particularly for those patients in whom treatment with ABC is being considered
- In white and black patients, screening for *HLA-B*5701* significantly reduces ABC-HSR
- 100% sensitivity

All HIV Positive Individuals Should Be Screened at Baseline for TB

- Patients without a history of tuberculosis or a prior positive tuberculosis screening test should be tested for *M. tuberculosis* infection by a tuberculin skin test (TST), preferably when the CD_4s count is >200.
- For an HIV-infected person, induration of >5 mm by TST is considered positive and a chest radiography and other evaluation, as warranted, to rule out active tuberculosis.
- A TST should be performed any time there is concern of a recent exposure to TB or after increase of CD_4 cell count to >200 cells/µL following initiation of ART

Other Diagnostic Test

- It is recommended that all patients receive a chest X-R at baseline, to asses for lung nodules and other lung conditions.
- All patients should be tested for prior exposure to *T. gondii* by measuring anti-Toxoplasma IgG upon initiation of care .
- An anti-CMV IgG should be done to assess for latent CMV infection.

Assessment of Viral Hepatitis

- Hepatitis B virus (HBV) infection should be assess upon initiation of care by detection of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and antibody to hepatitis B total core antigen (HBcAb)
- Those with HBsAb and HBcAb negative should be vaccinated for Hep B*
- Hepatitis C virus (HCV) infection should be assess upon initiation of care with a HCV antibody test, and every 6 months thereafter for those at risk .
- HCV RNA should be ordered on all those with a positive HCV antibody test to assess for active HCV disease.
- Hepatitis A total or IgG antibody should be done at initiation of care.
- Patients with negative antibody should receive vaccination for Hep A*

STI Screening in HIV Positive Patients

- All patients should be screened for syphilis upon initiation of care and every 6 months, depending on risk.
- In BC the preliminary screening test for syphilis is done with an Enzyme Immunoassay (EIA), a *Treponema pallidum*-specific antibody test.
- Men and women should be screened for gonorrhea and chlamydia infection at initial presentation and then annually if at risk for infections.
- All of these conditions should be screened for periodically thereafter, depending on the population, reported behaviors, the presence of other sexually transmitted infections (STIs) in the patient or his/her partner(s), and the prevalence of STIs in the community.

Schedule of HIV Specific Testing

	Test	Baseline	Follow-up Before ART	Follow-up After ART
Immuno-logical Assessment	CD_4 cell count (absolute and fraction)	✔	Every 3 to 4 months	Monthly until pVL undetectable and then every 3 to 6 months
HIV plasma viral load	Quantitative RNA testing	✔	Every 3-4 months	Monthly until pVL undetectable and then every 3 to 6 months
Drug resistance test	HIV genotype drug resistance	✔	At the time of initiation of ART	When pVL detectable and >200 c/ml, while on ART
Other	HLA- B*5701	✔	At baseline or at the time of initiation of treatment with Abacavir	On patients on Abacavir, not previously tested.
	Tropism Test It assess		When considering using CCR5 antagonist	

Other Blood Work Testing

	Test	Baseline	Frequency
Hematologic Assessment	CBC with Differential with CD_4 counts and HIV p-VL	✔	Every 3-4 months
Renal Function	Creatinine, eGFR, Urea Na, K, Cl, HCO_3 Urinalysis Urine for Abumin to Creatinine ratio (UACR)	✔	Every 3-4 months
Liver Function Tests	ALT, AST, T. bilirubin, INR	✔	Every 3-4 months
Blood Glucose	Fasting blood sugar Hg A1C	✔	Every 3-4 months Every 6 months
Lipid Profile	TC, LDL, HDL, Trig, Apo B	✔	Every 6 months
Hepatitis C	Total Antibody	✔	Every 6 months
Syphilis	RPR	✔	Every 6 months

Recommended Immunizations For HIV Positive Individuals

Hepatitis A Vaccine

- Give to all HIV positive susceptible (Hep A antibody -ve) patients
- Particularly important in patients at risk (IDU, MSM, hemophiliacs) or with chronic liver disease (e.g. HBV, HCV)
- Hepatitis A vaccine x 3 doses (0-1-6 months)

Hepatitis B Vaccine

- In all HIV positive susceptible (anti-HBs neg) patients
- Hep B vaccine x 3 doses of 20 mcg (10 mcg/ml) of Recombivax HB® or 40 mcg of Engerix B ® x 3 doses (0- 1- 6 months)
- Patients should have antibodies re-asses few months after completion of immunizations. If they have not developed antibodies, then they should receive additional 3 doses.

Pneumococcal Vaccine

- In individuals who have not previously received any pneumococcal vaccine: 1 dose of conjugate pneumococcal vaccine (Pneu-C-13) is followed at least 8 weeks later by 1 dose of polysaccharide pneumococcal vaccine (Pneu-P-23).
- In individuals who have received a pneumococcal vaccine previously: The Pneu-C-13 dose should be administered at least one year after any previous dose of Pneu-P-23.
- If re-immunization with Pneu-P-23 is needed, it should be given at least 8 weeks after the Pneu-C-13 dose and at least 5 years after the initial Pneu-P-23 dose.

Influenza Vaccination

- Annually regardless of CD_4 cell counts or HIV RNA levels
- Inactivated trivalent vaccine 0.5 mL IM
- May decrease CD_4 and increase pVL temporarily – not clinically relevant

Other Immunizations to Consider

- **Tetanus, diptheria (Td)**: Same recommendations as HIV-negative patients. Boost every 10 years with Td adsorb 0.5 mL IM.
- **Haemophilus influenzae type B**: In selected settings. Dose 0.5 mL IM. Administer to asplenic patients.
- **Herpes Zoster** :
  - Herpes zoster vaccine is contraindicated in HIV-positive individuals with CD_4 <200 cells/mm^3.
  - The use of herpes zoster vaccine for prevention of shingles in HIV-positive adults with CD_4 >200 cells/mm^3 is <u>not</u> routinely recommended

In general, live vaccines are not recommended in HIV-positive patients.

When are prophylaxes for opportunistic infections (OIs) recommended ?

They are only recommended when CD4 <200 and when the patient is unable or unwilling to start antiretroviral treatment.

Pneumocystis Jiroveci pneumonia (PJP) previously PCP Pneumonia

- **Primary Prophylaxis**
  - Recommended if:
    - CD_4 <200/mm^3 or <14%
  - TMP-SMX 1 SS/day
- **Secondary Prophylaxis (for patients who had PCP infection)**
  - Previous PCP (recovered)
  - TMP-SMX 1 DS/day

Mycobacterium Avium Complex (MAC) Prophylaxis Recommendations

When CD4 <50:

- Azithromycin 1200 mg once weekly

or

- Clarithromycin 500 mg BID (resistance more likely to develop than with azithro)

Primary Tuberculosis (TB) Prophylaxis in HIV

- **When PPD > 5 mm or prior TB exposure**
  - INH 300 mg + pyridoxine 50 mg qd x 9 mo
  - INH 900 mg + pyridoxine 100 mg twice weekly x 9 mo

Important Considerations

- The quality of the patient-provider relationship is often cited as one of the most important factors in a patient's engagement in care. Having a provider with whom the patient feels comfortable and can communicate effectively and frankly is key to developing this type of relationship .

- In addition, the multidisciplinary care model often helps to better retain patients in care, identify unmet care needs, and improve adherence to medications.

- Depression and substance abuse are highly prevalent in persons living with HIV infection. These two co-morbid conditions have been found to be important barriers to consistent adherence to ART and HIV care. Treatment of depression and management of the addictions can improve treatment adherence.

Summary

- All HIV positive patients need to have a primary care provided and a care plan.
- Past and present medical history, including relevant HIV related information and co-morbidities, should be obtained.
- Initial blood work should include CD_4 cell count , pVL, HLA-B*5701, baseline resistance test and standard blood test.
- Hepatitis A, B and C serology need to be updated at baseline and Hepatitis C serology should be repeated every 6 months in individuals at high risk who test negative for Hep C.
- Assessment for STIs is recommended at baseline, and syphilis test should be repeated every 6 months.
- Update immunizations according to present recommendations.
- Patients with CD_4 below 200 and not receiving ART should be on OI prophylaxis therapies.
- Assess and treat important co-morbidities, including depression and addictions.

Appendix 1: AIDS Defining Illnesses

- *Candidiasis* of bronchi, trachea, esophagus, or lungs
- *Invasive cervical cancer*
- *Coccidioidomycosis*
- *Cryptococcosis*
- *Cryptosporidiosis*, chronic intestinal (greater than 1 month's duration)
- *Cytomegalovirus* disease (particularly CMV retinitis)
- *Encephalopathy*, HIV-related
- *Herpes simplex*: chronic ulcer(s) (greater than 1 month's duration); or bronchitis, pneumonitis, or esophagitis
- *Histoplasmosis*
- *Isosporiasis*, chronic intestinal (greater than 1 month's duration)
- *Kaposi's sarcomav*
- *Lymphoma*, multiple forms
- *Mycobacterium avium complex*
- *Tuberculosis*
- *Pneumocystis carinii pneumonia*
- *Pneumonia*, recurrent
- *Progressive multifocal leukoencephalopathy*
- *Salmonella septicemia*, recurrent
- *Toxoplasmosis* of brain
- *Wasting syndrome* due to HIV

Appendix 2: Where to get information about management and treatment of HIV

- BC-CfE Primary Care Guidelines and Treatment Guidelines (pdf and mobile versions)

  http://education.cfenet.ubc.ca/bc-cfe-guidelines/

- Support telephone lines:
  - Primary care consults for physicians :
    - REACH Line available 24/7 (604-681-5748)
    - RACE Line available Mo-Fri 8 to 5 pm (604-696-2131)
  - Pharmacy support line: 1-888-511-6222